**Stephen J. Eglen,[1] Jay Demas,[2] and Rachel O.L. Wong[2]**
[1]Institute for Adaptive and Neural Computation
School of Informatics
University of Edinburgh
5 Forrest Hill
Edinburgh EH1 2QL
Scotland
[2]Department of Anatomy and Neurobiology
Washington University School of Medicine
St. Louis, Missouri 63110

**Selected Reading**

Bansal, A., Singer, J.H., Hwang, B.J., Xu, W., Beaudet, A., and Feller, M.B. (2000). J. Neurosci. *20*, 7672–7681.

Cohen-Cory, S. (2002). Science *298*, 770–776.

Debski, E.A., and Cline, H.T. (2002). Curr. Opin. Neurobiol. *12*, 93–99.

Grubb, M.S., Rossi, F.M., Changeux, J.-P., and Thompson, I.D. (2003). Neuron *40*, this issue, 1161–1172.

Hubel, D.H., and Wiesel, T.N. (1963). J. Physiol. *165*, 559–568.

Huberman, A.D., Stellwagen, D., and Chapman, B. (2002). J. Neurosci. *22*, 9419–9429.

Katz, L.C., and Crowley, J.C. (2002). Nat. Rev. Neurosci. *3*, 34–42.

McLaughlin, T., Torborg, C.L., Feller, M.B., and O'Leary, D.D.M. (2003). Neuron *40*, this issue, 1147–1160.

Penn, A.A., Riquelme, P.A., Feller, M.B., and Shatz, C.J. (1998). Science *279*, 2108–2112.

Ruthazer, E.S., Akerman, C.J., and Cline, H.T. (2003). Science *301*, 66–70.

Simon, D.K., and O'Leary, D.D.M. (1992). Brain Res. Dev. Brain Res. *69*, 167–172.

Simon, D.K., Prusky, G.T., O'Leary, D.D.M., and Constantine-Paton, M. (1992). Proc. Natl. Acad. Sci. USA *89*, 10593–10597.

Willshaw, D.J., and von der Malsburg, C. (1976). Proc. R. Soc. Lond. B. Biol. Sci. *194*, 431–445.

Wong, R.O.L. (1999). Annu. Rev. Neurosci. *22*, 29–47.

# Episodic Memory Signals in the Rat Hippocampus

**How does the hippocampus signal memory for episodes? In this issue of *Neuron*, Ferbinteanu and Shapiro show that classic place cell activity in the rat hippocampus together with robust retrospective and prospective memory signals reflects the sequence of past, present, and future events that make up an episode.**

Ever since Scoville and Milner (1957) hypothesized that damage to the hippocampus may underlie the profound memory deficit exhibited by patient H.M., intense research has focused on understanding the specific contributions of this structure to memory function. The discovery of place cells in the rat hippocampus by O'Keefe and Dostrovsky (1971) suggested that an understanding of the neurophysiological correlates of memory was within reach. However, the early emphasis on the idea that hippocampal place cells constitute a spatial map of the environment (cognitive map theory; O'Keefe and Nadel, 1978) led many researchers to focus on the spatial firing properties rather than on the memory correlates of hippocampal cells. Moreover, the view endorsed by the cognitive map theory, that the rat hippocampus is involved exclusively in spatial processing, was difficult to integrate with the classic findings that humans with medial temporal lobe damage exhibit long-lasting, multimodal memory impairments for facts and events.

More recently, a growing number of groups have started to examine the mnemonic correlates of rat hippocampal cell activity as animals perform various memory-demanding tasks. These studies clearly demonstrate that both spatial as well as nonspatial memory signals are observed in the rodent hippocampus. For example, Wood et al. (1999) recorded in the hippocampus as rats performed an olfactory delayed nonmatching to sample task. This study reported that more than half of the task-related activity was associated with nonspatial variables including olfactory-selective responses, as well as recognition memory signals. Other studies showed that place cell activity could be modulated by behavioral context including information about past or future behavior (Frank et al., 2000; Wood et al., 2000). These findings together with others led to the idea that the hippocampus signals a running record of the ongoing events in an episode irrespective of whether the information is spatial or nonspatial (memory space theory; Eichenbaum et al., 1999). However, none of the above-mentioned studies verified that task performance was dependent on intact hippocampal function or separated the influence of memory context from spatial trajectory.

To test the role of the hippocampus in signaling the on-going events in an episode, Ferbinteanu and Shapiro (2003) examined the mnemonic signals of hippocampal cells during the performance of a + maze alternation task impaired by fornix damage in rats. In this task, animals could start from either the north or south arm of the + maze and performed alternating blocks of trials where either the east or west arm was rewarded. Hippocampal activity was recorded as animals executed four possible journeys: north-east, north-west, south-east, or south-west (Figure 1). Between each trial, the animal was placed in a holding area, making the beginning and end of each journey distinct. Two major patterns of task-related activity were reported. The first was classic hippocampal place cell activity, which they term "journey-independent" spatial activity. These cells fired in a given location in the maze, irrespective of the journey taken on that trial (Figure 1B). The second major pattern of activity was termed "journey-dependent" spatial activity. Cells exhibiting this pattern of activity fired in a particular location on the maze only during a specific journey (i.e., activity on the north arm only during the north-east journey, but not during the north-west journey). Two different kinds of journey-dependent activity were described. The first type of journey-dependent activity was observed on the goal arm and was dependent on the identity of the start arm visited on that trial (Figure 1A). Thus, these cells signaled information about the previously visited place (retrospective signal). The second type of journey-dependent activity was observed

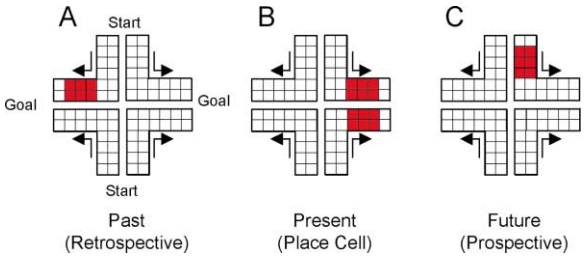


Figure 1. Neurophysiological Correlates of an Episode

Schematic representation of the three major patterns of activity observed on the + maze alternation task. Colored grids in (A)–(C) show the location of high activity on the + maze. Note that the activity for the four journey types are shown separately for the two start arms (north and south) and two goals arms (east and west) of the maze. (A) Example of journey-dependent retrospective pattern of activity. This cell responded in the west goal arm only on north-west journeys and not on south-west journeys. Thus, this cell signaled retrospective information about where the journey started. (B) Classic place cell activity. This cell responded in exactly the same place on the east arm, irrespective of where the journey started (journey-independent firing). (C) This cell provides a journey-dependent prospective signal, since it only responds in the start arm on north-east journeys but not on north-west journeys. In this way, networks of hippocampal cells convey information about the recent past (A), present (B), and imminent future (C).

on the start arm and was dependent on the goal arm about to be chosen (prospective signal; Figure 1C). Thus, hippocampal neurons signal information about the immediate past (retrospective signal) and the present (classic place cell activity) as well as the imminent future (prospective signal). Moreover, because about half of the journey-dependent cells in the goal arm maintained their spatial activity during "detour" trials when the path between the start and goal arm was not direct, this suggests that these cells did not depend on the spatial trajectory or the specific combinations of body movements made by the animal. Instead, this activity appears to signal selective information about particular goal-directed journeys.

Another key finding relevant to the interpretation of these retrospective and prospective signals is the analysis of activity during error trials. If these retrospective and prospective signals are important for task performance, then activity during error trials should be different compared to control trials. Ferbinteanu and Shapiro (2003) show that the responses of the populations of both prospective and retrospective cells were diminished on error trials. The diminished response on error trials was even more pronounced for the prospective signals than for the retrospective signal. This pattern is consistent with the idea that prospective signals may be more vulnerable to the effects of interference than retrospective signals that convey information about what just happened.

In summary, these findings provide striking new evidence that place cell activity coexists with equally prominent mnemonic signals for the recent past or immediate future to provide a continuous record of events that make up an episode. The results described in this study also highlight the important progress that has been made in the development of a rat model of human memory. As mentioned above, early theories of memory based on rat hippocampal physiology were difficult to relate to human findings because of their emphasis on spatial processing (O'Keefe and Nadel, 1978). In contrast, findings in humans emphasized the importance of the hippocampus in episodic memory, a form of memory that has been considered unique to humans (Tulving 2002). The new findings from Ferbinteanu and Shapiro show that, with clever task design and data analysis, the neurophysiological correlates of episodic memory can be identified and studied at the single-cell level. This approach constitutes a powerful animal model of human episodic memory.

**Wendy A. Suzuki**
Center for Neural Science
New York University
4 Washington Place, Room 809
New York, New York 10003

**Selected Reading**

Eichenbaum, H., Dudchenko, P., Wood, E., Shapiro, M., and Tanila, H. (1999). Neuron *23*, 209–226.

Ferbinteanu, J., and Shapiro, M.L. (2003). Neuron *40*, this issue, 1227–1239.

Frank, L.M., Brown, E.N., and Wilson, M. (2000). Neuron *27*, 169–178.

O'Keefe, J., and Dostrovsky, J. (1971). Brain Res. *34*, 171–175.

O'Keefe, J., and Nadel, L. (1978). The Hippocampus as a Cognitive Map (New York: Oxford University Press).

Scoville, W.B., and Milner, B. (1957). J. Neurol. Neurosurg. Psych. *20*, 11–21.

Tulving, E. (2002). Ann. Rev. Psych. *53*, 1–25.

Wood, E.R., Dudchenko, P., and Eichenbaum, H. (1999). Nature *397*, 613–616.

Wood, E.R., Dudchenko, P.A., Robitsek, R.J., and Eichenbaum, H. (2000). Neuron *27*, 623–633.

# Active Vision and Visual Activation in Area V4

**During normal vision, the focus of gaze continually jumps from one important image feature to the next. In this issue of *Neuron*, Mazer and Gallant analyze neural activity in higher-level visual cortex during this kind of active visual exploration, and they demonstrate a localized enhancement of visual responses that predicts the target of the upcoming eye movement.**

Vision science would be wonderfully simplified if the spatial relationship between the world and the retinal receptor sheet never changed. In fact, the idea is so appealing that most vision research is conducted as though this were the case. The angle of gaze is fixed, through anesthesia or behavioral control, and stimuli are presented at a single position on a display device. In real life, however, the angle of gaze continually jumps in a seemingly erratic pattern calculated to position the high-acuity fovea over important regions of the visual